

In the Specification

Please substitute the following paragraph on page 1, line 17:

Biocatalysis, defined as the biological synthesis of the molecules in question enzymatically, has been becoming more popular by offering a strong alternative to chemical synthesis, in terms of cost, time, purification steps, and simplicity of use. The introduction of any new biocatalysis process on an industrial scale necessitates, however, (i) identifying the enzyme (or the enzymes) which make(s) it possible to specifically convert the substrate provided into the desired product, (ii) identifying the enzyme (or the enzymes) which make(s) it possible to implement the catalysis in a stable manner and in the particular conditions linked to the industrial process (thermostability, pH, or tolerance to denaturation conditions of organic solvents, etc).

10541087
Jm
8/30/10

Please substitute the following paragraphs on page ¹7, line 31 to page ²7, line ¹³8:

However, the promising approach of exploiting these bacterial functions has always been considerably limited by a technological obstacle : the isolation and *in vitro* culture of the enormous potential offered by the bacterial diversity. Most bacteria developing in complex natural environments (soils and sediments, aquatic environments, digestive ~~systems, ... systems~~) have not been cultivated because their optimal culturing conditions are unknown or too difficult to reproduce. Numerous scientific works demonstrate this established fact, and it is now widely admitted that only between 0.1 and 1% of the bacterial diversity, including all environments, have been isolated and cultivated (Amann *et al*, 1995, Microb. Rev., 59 :143-169). Even if the search for novel biocatalytic pathways within collections of microbic strains has proved to be effective, it nevertheless has the major disadvantage of only exploiting a tiny part of the bacterial biodiversity.

New approaches have been developed in order to overcome this critical point of isolating bacteria ~~and~~ in order to gain access to this enormous genetic potential offered by the adaptation systems of bacteria developed over their long evolution. This approach is called Metagenomics because it relates to a set of genomes from a bacterial community without any distinction (metagenome).

Please substitute the following paragraph on page 5, line 1:

Another approach has already been described in patent WO 00/22170 of Microgenomics (N^o US Patent No. 6,368,793 B1). This patent describes a methodology for identifying a metabolic pathway transforming a substrate S into a desired product T by creating or identifying a genetically manipulated organism of which the capability of implementing this reaction is placed under the control of an inducible promoter. This organism is used for screening fragments of nucleic acids in order to detect a gene involved in the transformation of a substrate into a product. The implementation of this method requires the identification and genetic characterisation of the genes responsible for the degradation of T in the expression host so that they can be placed under the control of an inducible promoter. This type of construct ~~can not~~ cannot always be considered, in particular when the genes in question are spread over the genome and there is a possible risk of "leaking" into the inducer. On the other hand, it represents extremely hard work which has to be repeated for every study of a product T. Finally, in this approach, the organism used must be capable of incorporating and metabolising S and T. All of the elements mentioned demonstrate the limits of the efficacy of this type of approach.

DM
2/30/10 ³⁰
Please substitute the following paragraph on page 5, line 33 through page 6, line 2:

The time required and the means used to create the metagenomic library and then its screening ~~are~~ is therefore key, with small hope of success. An increase in the chances of discovery would involve, absolutely, the creation of a metagenomic library specific to each problem, in order to best respond to the objectives set.

Please substitute the following paragraph on page 13, line 24:

- transformed clones resulting from mutation, of phenotype (Ai- ; B-), having lost the capability of growing on {Ai} and on {B}. This change of phenotype can be explained either because (i) the metabolic pathway of {Ai} passes via {B} and the metabolism of {B} is disrupted (mutated phenotype IIIa), or because (ii) the mutagenesis has reached an element common to {Ai} and {B} such as for example a regulation element, a common transporter etc. (phenotype IIIb).

Art Unit: 1639

line 9, step c), "at least one" has been deleted
and replaced with ---said---

After substrate {Ai}, ----selected from the group
consisting of phytosterols, 1-phenyl-2-propanol
and mandelonitrile---- has been inserted.

line ¹⁴~~15~~, step d), "at least one" has been
deleted.

line ¹⁶~~15~~, "at least one" has been deleted.

Claim 25, line ⁶~~7~~, step 1), before library, ---metagenomic--
has been inserted.

Claim 32, line ¹~~2~~, before library, ---metagenomic--- has
been inserted.

Claim 33, line ¹~~2~~, before library, ---metagenomic--- has
been inserted.

Claims 21-24, 26-31 and 36 have been cancelled.